View metadata, citation and similar papers at core.ac.uk
brought to you by CORE
provided by Elsevier - Publisher Connector



**Program/Abstract # 291**
**Pleiotrophic roles for syndecan-4 in muscle regeneration**
Katie L. Capkovic, D.D.W. Cornelison
*Department of Biological Sciences, University of Missouri, Columbia, MO, USA*

Skeletal muscle regeneration in mammals requires the activity of satellite cells, a resident myogenic stem cell. Upon local injury, these cells must first be activated from a quiescent state, then proliferate extensively and migrate to the site of injury, and finally differentiate into replacement muscle fibers. While these four processes would be expected to require distinct extracellular signaling mechanisms, we have previously shown that a single transmembrane glycoprotein, syndecan-4, is required for appropriate activation, proliferation, and differentiation, and present new data suggesting that it is also required for migration (see poster #xx.) While it is a relatively small protein, syndecan-4 has been shown in other cell types to interact with a multitude of different extracellular (RTKs, GPCRs, integrins, ECM components, Wnt receptors, etc) and intracellular (small G proteins, cytoskeletal components, signaling adaptors, bioactive lipids, intracellular protein kinases, etc) factors and thereby alter cell signaling and activity via distinct protein motifs within the syndecan-4 intracellular domain. We have begun structure–function studies using domain-specific mutants of syndecan-4 to try to dissect the roles played by discrete signaling molecules and pathways in three of the four major satellite cell activities. By re-expressing labeled syndecan-4 (wild type or domain mutants) in primary satellite cells derived from syndecan-4 null mice and assessing the extent to which each aspect of the mutant phenotype is rescued, we hope to identify the critical pathway(s) required for each.

doi:10.1016/j.ydbio.2008.05.311

**Program/Abstract # 292**
**Role of Ldb1 in tissue homeostasis of the adult mouse**
Ipsita Dey-Guha, Mahua Mukhopadhyay, Heiner Westphal
*LMGD, NICHD, NIH, Bethesda, MD, USA*

Ldb1 is an obligatory co-factor of the LIM-homeodomain genes which are essential during development of the mouse embryo. Ablation of this gene has a very severe phenotype in embryos and affects a variety of tissues. Ldb1 is also widely expressed in the adult organism. In order to determine the role of this gene in the adult, we deleted the Ldb1 gene from the skin tissue. In normal skin, Ldb1 protein is prominently expressed in hair follicles and in the basal layer of the epidermis, resembling the expression pattern of the epithelial stem cell marker p63. Confirming previous reports, we see pronounced Ldb1 gene expression in keratinocytes located in the bulge region, the area of the epidermal stem cell niche. Tamoxifen-mediated ablation of the Ldb1 gene severely affects Ldb1 expression in these cells. This allows us to investigate the involvement of Ldb1 in the homeostasis of the adult skin. Our results further confirm a role of Ldb1 in maintaining tissue homeostasis in the adult mouse.

doi:10.1016/j.ydbio.2008.05.312

**Program/Abstract # 293**
**Islet1 and its cofactor LDB1 express in the mouse intestinal epithelium**
Evgeny Makarev, Heiner Westphal
*Laboratory of Mammalian Genes and Development, NIH, Bethesda, MD, USA*

Lim homeobox genes encode a family of transcription factors that have been conserved in evolution. They play prominent roles in tissue patterning and cell specification throughout development and also in the adult. The project described here concerns the function of *Lhx* and *Ldb1* gene products in the context of tissue homeostasis in the small intestine of the adult mouse. Our qPCR analysis revealed the presence of significant amounts of *Lhx1, Islet1, Islet2, Lmx1a, Ldb1* and *Ldb2* transcripts in the small intestine. Using antibodies against Ldb1 and Islet1 proteins it was found a unique pattern of expression of these genes in the gut. Ldb1 and Islet1 express in single cells in the small intestine in the crypt compartment of the gut. Co-localization experiments confirmed that Ldb1 and Islet1 expression overlaps in some cells. However, the pattern of Ldb1 expression is broader then Islet1 that means all Islet1 positive cells are Ldb1 positive but not vise versa. The cells are positive for cytokeratines that are specific for gut epithelia, but negative for CD45, thereby excluding the possibility that they represent lymphocytes known to be interspersed among the gut epithelia. Stainings with markers for Phospho-Histone3 and Cleaved Caspase3 failed to show a link between Ldb1/Islet1 expression and cell division or apoptosis, respectively. For functional analysis of Ldb1 we used Vil-Cre/Ldb1-loxP system to delete Ldb1 only in epithelial cells of the intestine. Mutant mice do not show any obvious phenotype, leaving open the possibility of redundancy of Ldb1 and Ldb2 proteins. In order to test this possibility we are using Vil-Cre/Ldb1-loxP system on Ldb2 −/− mice.

doi:10.1016/j.ydbio.2008.05.313

**Program/Abstract # 294**
**WNT/β-Catenin signaling maintains regenerating adult oral appendage organs and promotes stem cell expansion and de novo organ development**
Fei Liu, Thomas Andl, Yuhang Zhang, Sarah Millar
*Deparments of Dermatology and Cell and Developmental Biology, University of Pennsylvania, Philadelphia PA, USA*

WNT/β-catenin signaling is required for embryonic development of taste buds and teeth. We found this pathway is also active in taste buds and salivary glands of adult mice. To explore the potential of manipulating β-catenin signaling for regeneration of these oral tissues, we utilized K5-rtTA tetO-Dkk1 (loss-of-function, LOF) mice and K5-rtTA tetO-Cre Ctnnb1fl(ex3)/+ (gain-of-function, GOF) mice, in which inhibition or activation of Wnt signaling in oral epithelia can be induced with doxycycline respectively. In adult GOF mice induced for two weeks, multiple ectopic innervated taste buds expressing taste sensory markers were formed in each fungiform papilla. Multiple tooth-like structures with differentiated ameloblasts and odontoblasts were formed at the labial side of incisors in these GOF mice, and expression of embryonic tooth bud markers in these structures indicated de novo tooth development. In GOF submandibular salivary glands (SMG), mucous acini were replaced by proliferating duct structures, and expression of progenitor cell markers was upregulated. Conversely, in LOF mice induced for 6months, mucous acini of SMG were hyper-proliferative, taste bud structures and taste sensory cell markers were lost from most fungiform papillae, and ameloblasts disappeared from the labial side of incisor teeth. Our findings indicate that WNT/β-catenin signaling is required for maintenance of regenerating oral appendage organs, and can promote stem cell expansion and de novo organ development in adult oral cavity when stimulated.

doi:10.1016/j.ydbio.2008.05.314